In vitro differentiation of hESCs into corticospinal motor neurons

Grant Award Details

In vitro differentiation of hESCs into corticospinal motor neurons

Grant Type: SEED Grant

Grant Number: RS1-00170

Investigator:

Name:	Bin Chen
Institution:	University of California, Santa Cruz
Type:	PI

Disease Focus: Amyotrophic Lateral Sclerosis, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $465,624

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: In vitro differentiation of hESCs into corticospinal motor neurons

Public Abstract:

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, fatal neurological disease that leads to the degeneration of motor neurons in the brain and in the spinal cord. There are currently 20,000 ALS patients in the United States, and 5,000 new patients are diagnosed every year. Unfortunately no cure has been found for ALS. The only medication approved by the FDA to treat ALS can only slow the disease's progression and prolong life by a few months in some patients. Thus it is critical to explore other therapeutic strategies for the treatment of ALS such as cell replacement strategy.

Because of the ability to generate many different cell types, human embryonic stem cells (hESCs) may potentially serve as a renewable source of cells for replacing the damaged cells in diseases. However, transplanting ESCs directly may cause tumor growth in patients. To support cell transplants, it is important to develop methods to differentiate hESCs into the specific cell types affected by the disease. In this application, we propose to develop an effective method to differentiate hESCs into corticospinal motor neurons (CSMNs), the neurons in the cerebral cortex that degenerate in ALS. We will test whether these CSMNs generated from hESCs in culture conditions can form proper connections to the spinal cord when transplanted into mouse brains.

To direct hESCs to become the CSMNs, it is critical to establish a reliable method to identify human CSMNs. Recent progress in developmental neuroscience have identified genes that are specifically expressed in the CSMNs in mice. However no information is available for identifying human CSMNs. We hypothesize that CSMN genes in mice will be reliable markers for human CSMNs. To test this hypothesis we will investigate whether mouse CSMN markers are specifically expressed in the human CSMNs.

The therapeutic application of hESCs to replace damaged CSMNs in ALS depends on the ability to direct hESCs to develop into CSMNs. Currently a reliable condition to direct hESCs to differentiate into CSMNs has not been established. We will attempt to differentiate hESCs into CSMNs based on the knowledge gained from studying the development of nervous system. We will achieve this goal in two steps: first we will culture hESCs in a condition to make them become progenitors cells of the most anterior region of the brain; then we will culture these progenitors to become neurons of the cerebral cortex, particularly the CSMNs. We will study the identities of these neurons using the CSMN markers that we have proposed to identify.

To apply the cell replacement strategy to treat ALS, it will be critical to test if human CSMNs generated from cultured hESCs can form proper connections in an animal model. We will transplant the CSMNs developed from hESCs into the brains of mice and test whether they can form connections to the spinal cord.

When carried out, the proposed research will directly benefit cell replacement therapy for ALS.

Statement of Benefit to California:	Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, fatal neurological disease that leads to the degeneration of motor neurons in the brain and in the spinal cord. There are currently 20,000 ALS patients in the United States, and 5,000 new patients are diagnosed every year. Unfortunately no cure has been found for ALS. The only medication approved by the FDA to treat ALS can only slow the disease's progression and prolong life by a few months in some patients. Thus it is critical to explore other therapeutic strategies for the treatment of ALS such as cell replacement strategy. Because of the ability to generate many different types of cells, human embryonic stem cells (hESCs) may potentially serve as a renewable source of cells for replacing the damaged cells in diseases. However, transplanting ESCs directly may cause tumor growth in patients. To support cell transplants, it is important to develop methods to differentiate hESCs into the specific cell types affected by the disease. In this application, we propose to develop an effective method to differentiate hESCs into corticospinal motor neurons (CSMNs), the neurons in the cerebral cortex that degenerate in ALS. We will test whether these CSMNs generated from hESCs in culture conditions can form proper connections to the spinal cord when transplanted into mouse brains. Everyday, 15 people die from ALS. For patients diagnozied with ALS, time is running out very fast. It is critical to explore novel therapeutic strategies for this rapidly progressive and fatal disease. The research proposed in this application may provide the basis for a novel cell replacement therapy for ALS, thus it will greatly benefit the State of California and everyone in the State.